California Institute for Regenerative Medicine

Analysis of a transgenic Oct4 enhancer reveals high fidelity long-range chromosomal interactions.

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Authors: Mingyang Cai, Fan Gao, Peilin Zhang, Woojin An, Jiandang Shi, Kai Wang, Wange Lu

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Public Summary:
Genome structure or nuclear organization has fascinated researchers investigating genome function. Recently, much effort has gone into defining relationships between specific genome structures and gene expression in pluripotent cells. Overall, this work reveals critical features that may function in gene expression regulation in mouse pluripotent cells.

Scientific Abstract:
Genome structure or nuclear organization has fascinated researchers investigating genome function. Recently, much effort has gone into defining relationships between specific genome structures and gene expression in pluripotent cells. We previously analyzed chromosomal interactions of the endogenous Oct4 distal enhancer in pluripotent cells. Here, we derive ES and iPS cells from a transgenic Oct4 distal enhancer reporter mouse. Using sonication-based Circularized Chromosome Conformation Capture (4C) coupled with next generation sequencing, we determined and compared the genome-wide interactome of the endogenous and transgenic Oct4 distal enhancers. Integrative genomic analysis indicated that the transgenic enhancer binds to a similar set of loci and shares similar key enrichment profiles with its endogenous counterpart. Both the endogenous and transgenic Oct4 enhancer interacting loci were enriched in the open nucleus compartment, which is associated with active histone marks (H3K4me1, H3K27ac, H3K4me3 and H3K9ac), active cis-regulatory sequences (DNA hypersensitivity sites (DHS)), 5-hydroxymethylcytosine (5-hmc), and early DNA replication domains. In addition, binding of some pluripotency-related transcription factors was consistently enriched in our 4C sites, and genes in those sites were generally more highly expressed. Overall, our work reveals critical features that may function in gene expression regulation in mouse pluripotent cells.

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